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INDOLE ALKALOIDS IN AMAZONIAN MYRISTICACEAE: FIELD AND LABORATORY RESEARCH

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BOTANICAL CONSIDERATIONS

Indians of the Amazon—especially of the northwest Amazon—and of adjacent parts of the Orinoco have employed various species of the myristicaceous genus Virola for many years as the bases of hallucinogenic preparations. A resin-like liquid of the inner bark of the trees is elaborated into an intoxicating snuff and is prepared in pellets for oral consumption; it is even on occasion ingested raw without any preparation.

Although undoubtedly a custom of great age, discovery of the use of Virola as an important hallucinogen is recent. In the early part of this century, the German anthropologist Theodor Koch-Grünberg reported that the Yekwana Indians of the Orinoco of Venezuela were utilizing an intoxicating snuff prepared from the "bark of a tree." He wrote that, when the bark was "pounded up, it is boiled in a small earthenware pot, until all the water has evaporated and a sediment remains at the bottom of the pot. This sediment is toasted in the pot over a slight fire and is then

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finely powdered with the blade of a knife." It was called *hakudufha* by the Yekwana (Koch-Grünberg 1923).

In 1938, the Brazilian botanist Adolpho Ducke indicated that, in the Rio Negro, the Brazilian Indians made a snuff called *paricá* from the leaves of *Virola theiodora* and *V. cuspidata* (Ducke 1938; 1939).

The source of the narcotic snuff was, however, not definitively identified until 1954, when voucher specimens and field studies indicated that the leaves are not used but that a bark exudate is the real source of the snuff. At that time, the Indians of the Río Apaporis of Amazonian Colombia were found to be using in ritual ceremonies of the medicine men an intoxicating snuff made from the red "resin" of the inner bark or from scrapings of the inner bark itself of *Virola calophylla, V. calophylloidea* and possibly *V. elongata* (Schultes 1954).

Later, it was learned that the Witoto Indians of Colombia did not utilize the red "resin" of the bark in the form of snuff but did value it in pellets orally ingested as a magic and ceremonial hallucinogen (Schultes 1969; Schultes and Swain 1976). More recent field work amongst the Boras and Witotos of Peru has indicated the use of *Virola Pavonis* and *V. elongata* as well as possibly *V. surinamensis* and *V. loretensis.* The Boras likewise point out *Iryanthera macrophylla* of a related myristicaceous genus as the source of a narcotic paste. This represents the first time that a genus other than Virola has been known to be involved in the myristicaceous hallucinogens of tropical South America.

Reports from the field work of an anthropologist—Peter L. Silverwood-Cope—inform us that the primitive, nomadic Makú Indians of the Río Piraparaná in Amazonian Colombia drink the "resin" directly, with no preparation and no admixture, for its hallucinatory effects (Schultes 1978, 1979).

There are suggestions that the bark of *Virola sebifera* may be smoked in Venezuela. Several herbarium collections note that the inner bark is smoked by witch doctors at dances when curing fevers and that they boil the bark "to drive away evil spirits." (Schultes and Hofmann 1980).

It is now known that a number of species of Virola are employed hallucinogenically in Brazil, Colombia, Peru and Venezuela: *V. calophylla, V. calophylloidea, V. cuspidata, V. elongata, V. Pavonis, V. surinamensis* and *V. theiodora* (Schultes and Hofmann 1979; 1980).

The hallucinogenic constituents are believed to be present in the almost colourless exudate from the inner surface of the outer bark which appears as soon as the bark is stripped from the tree. This exudate rapidly darkens to a reddish brown in a typical oxidase type reaction and dries to a hard shiny mass. In specimens of bark dried for chemical examination, it appears as a sticky, dark reddish brown, gummy material which has been shown to contain tryptamines and other indolic hallucinogens (Agurell, Holmstedt, Lindgren and Schultes 1968; 1969).

It has been observed, however, that the only reason for scraping the inner surface of the bark (phloem) is to obtain all traces of cambium which might adhere to it. The drug itself, whether snuff or pellets, is prepared from the cambial sap only, which is first quickly boiled, causing coagulation of protein and perhaps polysaccharides, and then simmered slowly to reduce the volume to near dryness. This gives the sticky brownish material from which the "resin" snuff or pellets are prepared. The whole process is similar to that used for the isolation of other natural products from the cambium of other trees, such as coniferin from gymnosperms, for example; except that today one would employ ethyl alcohol or acetone, rather than heat, to destroy enzyme activity which might otherwise act adversely on the desired product (Schultes and Swain 1976).

Virola *Aublet*

A tropical American genus of 45 to possibly 60 species of tropical forest trees widely distributed in Central and South America, Virola is abundant, especially in the Amazon, where it is esteemed as the source of an hallucinogen, in native medicine and as the basis of an arrow poison (Schultes and Holmstedt 1968, 1971; Prance 1970).

Virola is generally known as *cumala* in the Peruvian Amazon: various species are distinguished as *cumala blanca, cumala roya,* *cumala caspi.* In Brazil, the general name for Virola is *ucuúba-ucuúba branca, ucuúba preta, ucuúba vermelha.* The Venezuelan species have many vernacular names: *camaticaro, cedrillo, cozoiba, cuajo, cuajo negro, cudo rebalsero, sangerino, trompillo.* In Colombia, the most widely used common name is *cuajo,* although in the Amazonian regions this term is rarely employed.

Native names for species of Virola are many. The most frequently met with in the literature, mainly because of the use of the plants as hallucinogens, are *yakee* (Puinave), *yato* (Kuripako) in Colombia; *epena* or *nyakwana* (Waika) in Brazil and Venezuela; *paricá* (Tukano) in Brazil and Colombia; *oo-koó-na* (Witoto) in Colombia and Peru; *krüdeeko* (Bora) in Peru. In Amazonian Colombia, the Yukunas know *V. calophylla* as *are-de-yé*; the Barasanas as *yeag aseiiñ*. The Kubeo call *V. calophylloidea ko-gá*; the Barasanas, *rose-nameti.* They refer to the related *V. elongata* by the slight variant: *rose-nemee. V. peruviana* is called *râ-pa* by the Kabuyarí Indians of the Río Apaporis. The Barasanas know *V. carinata* as *nat-sin-neme;* the Makús, as *bon-amí*; the Makunas, as *lasil-me-je-ju.*

The family Myristicaceae was originally treated as monogeneric. The concept Virola, proposed by Aublet in 1775, was included in the genus Myristica. Many of the species now considered to represent Virola were described by Spruce or Spruce and Bentham as belonging to Myristica. In his letters and field notes, Spruce frequently referred to Virolas as "nutmegs," as the well known source of the spice nutmeg is *Myristica fragrans.* When Warburg published his monumental monographic studies on the family Myristicaceae in 1897, he restricted Myristica to Old World representatives and recognized as a valid concept Aublet's Virola, into which he transferred a large number of species which, until then, had been accommodated in Myristica. The same specialist set up to accommodate other tropical American myristicaceous species earlier described as Myristica the new generic concepts of Compsoneura, Dialyanthera, Iryanthera and Osteophloem. Subsequent taxonomists have accepted Warburg's treatment of the generic composition of the family: A. C. Smith, Adolpho Ducke and William Rodrigues. It appears that the most important species of Virola for the preparation of the halluci-nogenic snuff or paste is *V. theiodora.*

Virola theiodora occurs mainly in the western Amazonia of Brazil and Colombia, possibly also in adjacent parts of Peru and Venezuela. It is especially abundant in the Rio Negro drainage-area. The tree is normally found in well drained forests.

The analyses which follow have been carried out on material without regard as to whether or not it enters into native hallucinogenic preparations.

CHEMICAL CONSIDERATIONS

In 1977, the Alpha-Helix Amazon Expedition 1976-1977, Phase VII, dedicated to *Ethnopharmacological Studies of the Flora and Fauna of the Pebas Region of the Peruvian Amazon,* presented an unparalleled opportunity to study the use of orally administered paste prepared from Virola among the Bora and Witoto Indians of the area and to investigate plants and derivatives of plants in the fully equipped chemical laboratory on board. One of the projects undertaken by Phase VII constituted ethnopharmacological and chemical studies of various local species of Virola and, to a lesser extent, of the allied genera Iryanthera and Osteophloeum.

These studies are of interest, partly because the material analyzed was, in all cases, fresh, partly because some of the species studied had never been subjected to chemical investigation and partly because several of them were formerly employed by the Bora and Witoto Indians of the region in their magico-religious rituals and witchcraft.

The material collected during the 1977 Alpha-Helix expedition was preserved in a freezer (dark, −40° C) until analyzed. Most of these specimens of Virola were collected in the Río Ampiyacu and Río Yaguasyacu region and also near Pebas (Río Amazonas, Peru).

Reference Compounds

The reference compounds have been synthesized as described earlier (Agurell *et al.* 1969).

Isolation of Alkaloids

The powdered plant material (1–20 g) was extracted with methanol. After filtration and evaporation, equivalent amounts of $CHCl_3$ and O,1-N HCl were added, and the organic layer was discarded after shaking. The aqueous layer was washed with $CHCl_3$ and was then made alkaline (pH = 9.0) with solid Na_2CO_3. The liberated organic bases were extracted with $CHCl_3$. The dried extract was dissolved in a suitable amount of mixture MeOH/$CHCl_3$ (1:1) and submitted to TLC, GC and GC-MS analyses.

Thin-layer Chromatography (TLC)

Alkaloid constituents were separated on Silica Gel G TLC ready made plates (Merck No. 5748) with methanol-ammonia (99:1) as solvent. Alkaloids were located with Dragendorff's reagent and tryptamines with Erlich's reagent.

Gas Chromatography (GLC)

Gas chromatographic analysis was performed with two commerical apparatus (Pye Unical Model 104 and Schimadzu Model GC mini-1), equipped with hydrogen flame ionization detection systems.

The stationary phases used were:

1) 3% SE—30 ultraphase (1,50 m × 2.0 mm glass tube);
2) 3% OV—17 ultraphase (1,50 m × 2.0 mm glass tube);
3) SE—30 capillary WCOT column (25 m × 0.2 mm glass tube).

The columns were operated with temperature programming from 150° to 280° at 5°/min. rate. The injector block and the detector chamber were kept at 300°. For capillary column, a "solvent free" injection device was used (van den Berg and Cox 1972).

The amount of alkaloids in mg/100 g plant material and the percentage of each alkaloid in the alkaloid mixture was determined with the capillary column using DMT as a standard.

Gas Chromatography-Mass Spectrometry (GC-MS)

The principles of the technique have been described earlier (Holmstedt and Lindgren 1967). The mass spectrometry work was carried out with an LKB 2091 gas chromatograph-mass spectrometer. The ion source was at 270°, the electron energy was 70 e V and the electron ionization current 50 μA, respectively. The separations were made on columns consisting of 3% SE-30 and 3% OV-17 (2 m × 2.0 mm glass tube) with temperature programming.

List of chemical abbreviations used

DMT	=	N,N-Dimethyltryptamine
MMT	=	N-Methyltryptamine
T	=	Tryptamine
5-MeO-DMT	=	5-Methoxy-N,N-dimethyltryptamine
5-MeO-MMT	=	5-Methoxy-N-methyltryptamine
MTHC	=	2-Methyl-1,2,3,4-tetrahydro-β-
	=	carboline
6-MeO-THC	=	2-Methyl-6-methoxy-1,2,3,4-tetra-
	=	hydro-β-carboline
6-MeO-DMTHC	=	1,2-Dimethyl-6-methoxy-1,2,3,4-te-
	=	trahydro-β-carboline

Comments on Chemical Constituents of Virola and Related Genera

Fifty-three voucher collections of Virola and related genera made by various botanists over a time span of several decades have been analyzed for alkaloids. Of the total number of collections, 18 proved negative when analyzed for alkaloids in various parts of the plant. Occasionally, different collections representing the same species have proven to be alkaloid-positive in some cases and negative in others. Four analyses of different collections of *Virola surinamensis,* however, all proved to be negative.

To our knowledge, only the bark and/or constituents of bark are used in the preparation of the intoxicating snuffs employed by the Indians. The alkaloid content of bark specimens is listed in Table 1, which also gives the species used in the manufacture of snuffs and the approximate alkaloidal content.

From this table, it is apparent that the species used are usually rich in alkaloids. *Virola rufula* is not known to be employed and, if it is not utilized, it would appear that the Indians have missed an alkaloid-rich species. In addition to the bark, the leaves and flowering shoots seem to be usually rich in alkaloids.

The simple alkaloids MMT, DMT, 5-MeO-MMT and 5-MeO-DMT abound in the species used; they are also present in other species.

The nyakwana snuff analyzed by Agurell *et al.* (1969) proved to be extraordinarily rich in base content (11%). This might explain

Table 1

Distribution of indole alkaloids in Virola sp. and related genera

Collection	Species	Part of Plant	Alkaloids: mg/100 g a) D. W. b) F. W.	Alkaloids	%
Schultes 24603	*Virola calophylla*[3] Manáos, Brazil	Bark	9 a)	DMT 5-MeO-DMT	91 9
		Root	1 a)	DMT 5-MeO-DMT	87 13
		Leaves	155 a)	MMT DMT	4 96
		Flowers Shoots	193 a)	MMT DMT	4 96
Plowman, Schultes & Tovar 6789	*Virola calophylla* Pebas, Peru (Alpha-Helix 1977)	Bark		DMT MMT MTHC	
Prance 14947	*Virola calophylla* Rio Cuieras, Brazil	Bark	9 a)	DMT 5-MeO-DMT	
		Root	1 a)	DMT 5-MeO-DMT	
		Leaves	115 a)	MMT DMT	
Plowman, Schultes & Tovar 7093	*Virola calophylloidea* Pebas, Peru (Alpha-Helix 1977)	Bark	7.5 b)	DMT 5-MeO-DMT 5-MeO-MMT	50 45 5
Prance 14312	*Virola calophylloidea* Rio Curuquete, Brazil	Leaves	1.35 a)	DMT	100
Prance 14954	*Virola calophylloidea* Rio Cuieras, Brazil	Leaves	98 a)	DMT	100
Schultes & Rodrigues 26181a	*Virola carinata* Manáos, Brazil	Leaves Bark Twigs 1)	0.04 a)	DMT	100
Prance 13994	*Virola cuspidata* Rio Ituxi, Brazil	Leaves	neg. 2)		
Prance 15120	*Virola cuspidata* Rio Negro (middle course), Brazil	Leaves	neg. 2)		

Collection	Species	Part of Plant	Alkaloids: mg/100 g a) D. W. b) F. W.	Alkaloids	%
Schultes & Rodrigues 26115a	*Virola divergens* Manáos, Brazil	Leaves Bark 1)	0.5 a)	DMT	100
Plowman, Schultes & Tovar 6595	*Virola elongata* Pebas, Peru (Alpha-Helix 1977)	Leaves Bark Stem	neg. 2) neg. neg.		
Plowman, Schultes & Tovar 6920	*Virola elongata* Pebas, Peru (Alpha-Helix 1977)	Phloem		T DMT MMT MTHC 5-MeO-DMT 5-MeO-MMT	
		"Resin"		T MMT DMT MTHC	
		Leaves	neg. 2)		
		Wood	neg.		
Plowman, Schultes & Tovar 7263	*Virola elongata* Pebas, Peru (Alpha-Helix 1977)	Paste		5-MeO-DMT 6-MeO-THC	
		Phloem		5-MeO-DMT	100
		Wood	neg. 2)		
Plowman, Schultes & Tovar 7092	*Virola elongata* Pebas, Peru (Alpha-Helix 1977)	Bark	3.2 b)	MMT DMT T 5-MeO-DMT 5-MeO-MMT MTHC	81 14 4 trace trace trace
Prance 15310	*Virola elongata* Tapurucuara, Rio Negro, Brazil	Leaves	19 a)	DMT	100
Plowman, Schultes & Tovar 7144	*Virola loretensis* Pebas, Peru (Alpha-Helix 1977)	Bark	neg. 2)		
Plowman, Schultes & Tovar 259	*Virola loretensis* Pebas, Peru (Alpha-Helix 1977)	Bark	neg. 2)		

Table 1 (*continued*)

Collection	Species	Part of Plant	Alkaloids: mg/100 g a) D. W. b) F. W.	Alkaloids	%
Prance 11035	*Virola Melinonii* Rio Mucajaí, Roraima, Brazil	Leaves	neg. 2)		
Schultes & Rodrigues 26153a	*Virola Melinonii* Manáos, Brazil	Bark	0.18 a)	DMT	100
Schultes 24614	*Viola multinervia* 3) Manáos, Brazil	Bark	1 a)	DMT	100
		Root	1 a)	DMT 5-MeO-DMT	41 59
Schultes 24616	*Virola multinervia* 3) Manáos, Brazil	Bark	1 a)	DMT	100
Schultes & Rodrigues 26151a	*Virola multinervia* Manáos, Brazil	Bark	neg. 2)		
Plowman, Schultes & Tovar 6682	*Virola peruviana* Pebas, Peru (Alpha-Helix 1977)	Bark		DMT 5-MeO-DMT 6-MeO-THC 6-MeO-DMTHC	
Plowman, Schultes & Tovar 6890	*Virola peruviana* Pebas, Peru (Alpha-Helix 1977)	Paste	27.6 b)	5-MeO-DMT 6-MeO-THC 6-MeO-DMTHC	99 trace trace
Plowman, Schultes & Tovar 6900	*Virola peruviana* Pebas, Peru (Alpha-Helix 1977)	Paste	1.73 b)	5-MeO-DMT	100
Schultes 24612	*Virola rufula* 3) Manáos, Brazil (Alpha-Helix 1967)	Bark	200 a)	DMT 5-MeO-DMT	4 95
		Root	144 a)	DMT 5-MeO-MMT 5-MeO-DMT	1 4 94
		Leaves	98 a)	MMT DMT	6 94
Prance 12308	*Virola sebifera* Serra da Moa, Acre, Brazil	Leaves	neg. 2)		

Collection	Species	Part of Plant	Alkaloids: mg/100 g a) D. W. b) F. W.	Alkaloids	%
Plowman, Schultes & Tovar 6198	*Virola surinamensis* Pebas, Peru (Alpha-Helix 1977)	Bark	neg. 2)		
Plowman, Schultes & Tovar 6619	*Virola surinamensis* Pebas, Peru (Alpha-Helix 1977)	Bark	neg. 2)		
		Leaves	neg. 2)		
		Seed	neg. 2)		
		Aril	neg. 2)		
Plowman, Schultes & Tovar 6684	*Virola surinamensis* Pebas, Peru (Alpha-Helix 1977)	Bark	neg. 2)		
		Leaves	neg. 2)		
Plowman, Schultes & Tovar 6775	*Virola surinamensis* Pebas, Peru (Alpha-Helix 1977)	Bark	neg. 2)		
		Paste	neg. 2)		
Schultes 24595	*Virola theiodora* 3) Manáos, Brazil (Alpha-Helix 1967)	Bark	250 a)	MMT	1
				DMT	52
				5-MeO-DMT	43
				5-MeO-THC	4
		Root	17 a)	DMT	22
				5-MeO-MMT	15
				6-MeO-DMT	62
		Leaves	44 a)	DMT	100
		Flowers Shoots	470 a)	MMT	7
				DMT	93
Schultes 24626	*Virola theiodora* 3) Tototobí, Roraima, Brazil	Bark	65 a)	DMT	5
				5-MeO-DMT	95
		Leaves	21 a)	DMT	98
				MTHC	2
Schultes 24613	*Virola venosa* 3) Manáos, Brazil (Alpha-Helix 1967)	Bark	neg. 2)		
		Root	1 a)	5-MeO-DMT	100
		Leaves	1 a)	DMT	100
Plowman, Schultes & Tovar 7091	*Virola venosa* Pebas, Peru (Alpha-Helix 1977)	Bark	neg. 2)		
Plowman, Schultes & Tovar 7094	*Virola* sp. indet. aff. *venosa* Pebas, Peru	Bark	7.2 b)	5-MeO-DMT	58
				MMT	20
				5-MeO-MMT	16

Table 1 (*continued*)

Collection	Species	Part of Plant	Alkaloids: mg/100 g a) D. W. b) F. W.	Alkaloids	%
Plowman, Schultes & Tovar 7094	(Alpha-Helix 1977)			DMT	6
				T	trace
				6-MeO-THC	trace
				6-MeO-DMTHC	trace
		Leaves	14.7 b)	MMT	90
				DMT	8
				5-MeO-DMT	2
Schultes & Rodrigues 26188a	*Virola* sp. Manáos, Brazil	Leaves Bark Twigs 1)	0.22 b)	DMT	100
Schultes 26127	*Virola* n. sp. (?)	Leaves	0.07 a)	DMT	100
Schultes 26130	*Virola* sp.	Leaves Twigs 1)	neg. 2)		
Schultes & Rodrigues 26116	*Compsoneura Ulei* Manáos, Brazil	Leaves	neg. 2)		
Schultes & Rodrigues 26114	*Iryanthera coriacea* Manáos, Brazil	Leaves Bark Twigs 1)	neg. 2)		
Plowman, Schultes & Tovar 6919	*Iryanthera Ulei* Pebas, Peru (Alpha-Helix 1977)	Bark	0.013 b)	5-MeO-DMT	100
Plowman, Schultes & Tovar 7095	*Osteophloem platyplyllum* Pebas, Peru (Alpha-Helix 1977)	Bark	neg. 2)		
Schultes & Rodrigues 26126	*Osteophloem platyphyllum* Manáos, Brazil	Bark	0.62 a)	DMT 5-MeO-DMT 5-OH-DMT	
Prance 11117	*Osteophloem platyphyllum* Rio Mucajaí, Brazil	Leaves	neg. 2)		

1) The materials were mixed in a can containing alcohol.
2) Tested with Dragendorff and Ehrlich Reagents.
3) Published earlier by Agurell *et al.* (1969).

why the resin of *Virola theiodora* is also employed as an arrow poison. As has been pointed out by Gottlieb (1979) and as is evident from Table 1, there exist appreciable differences in the base composition of different parts of a single plant (Agurell *et al.,* 1969); this is true also of different species and even in analyses of different specimens representing the same species. When examining the data of Table 1 with respect to use, it must be kept in mind that the preparation of snuffs, pellets and arrow poison involves concentration of the resinous bark exudate to a thick syrup which is subsequently dried, powdered or rolled into pellets which are then coated with the residue of leachings from ashes. Such treatment, not to speak of storage, would be expected to alter the original base composition.

The hallucinogenic myristicaceous snuffs of the South American Indians owe their biological activity to the simple methylated indoles mentioned above (Holmstedt and Lindgren 1967; Agurell *et al.* 1969). Bufotenine, a component of the snuff made from *Anadenanthera peregrina* (Chagnon *et al.* 1971) is not present in the species of Virola investigated; neither is it present in the snuff made from them.

When analyzing Indian snuffs in 1967, Holmstedt and Lindgren noted the presence of harmala alkaloids in several preparations of uncertain botanical origin. In one case, both the simple indoles and harmine were present in the same preparation. This observation led to the following conclusion:

"In South American botany, β-carbolines (harmine, harmaline and tetrahydroharmine) are usually associated with the species of Banisteriopsis, wherefore it is very likely that this is their origin in the snuffs. Very likely this is an admixture to the snuff, although definite botanical proof for it is lacking at the moment. To the knowledge of the authors, simple indoles and β-carbolines have not yet been isolated *from the same plant*.

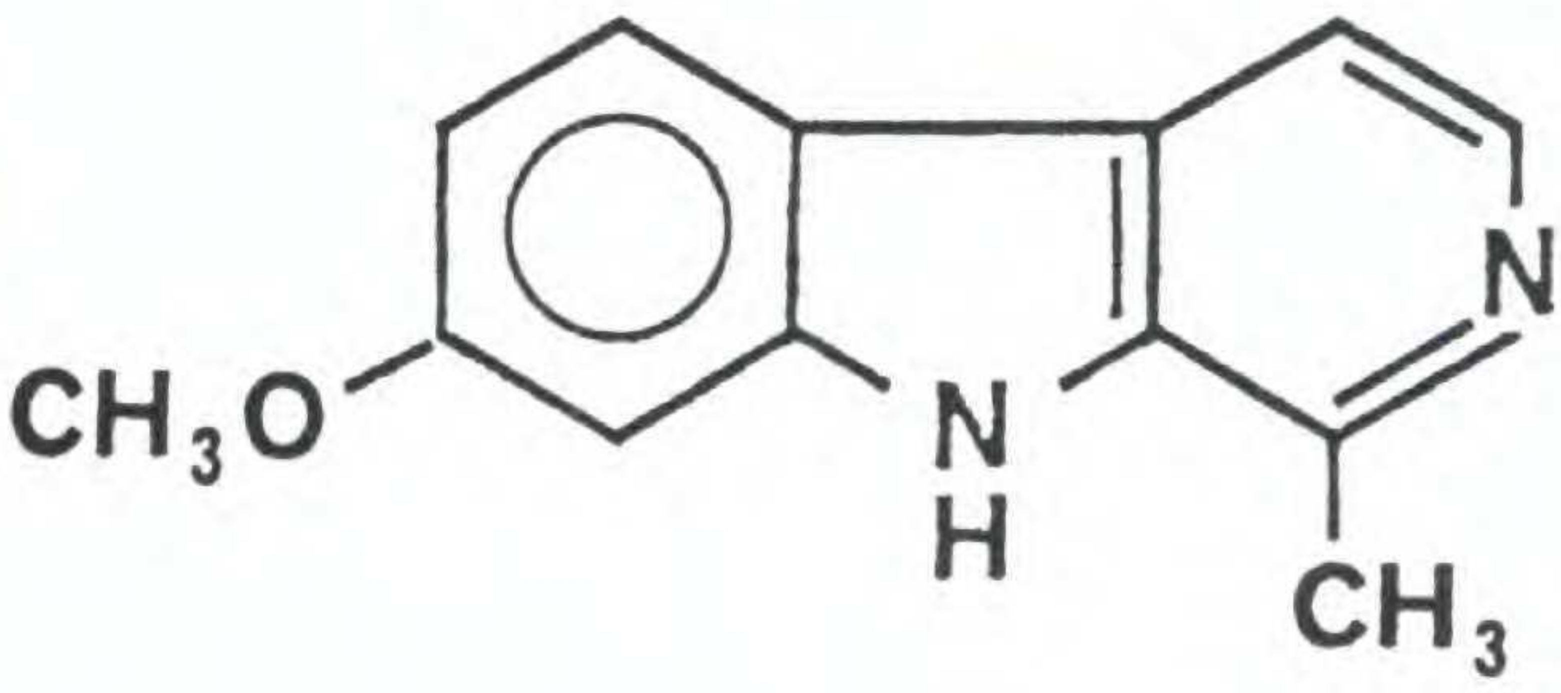
"The occurrence of both tryptamines and β-carbolines in the South American snuffs is pharmacologically interesting. The β-carbolines such as harmine and harmaline (Fig. 1) are monoamineoxidase inhibitors (Udenfriend *et al.* 1958) and could potentiate the action of the simple indoles. The combination of β-carbolines and tryptamines would thus be advantageous.

However, pharmacological action of the β-carbolines unrelated to monoamineoxidase inhibition has also been proven to exist (Schievelben *et al.* 1966). Further botanical and chemical studies are obviously needed to see if the two groups of compounds in the snuff are derived from one plant or a mixture of plants" (Holmstedt and Lindgren 1967).

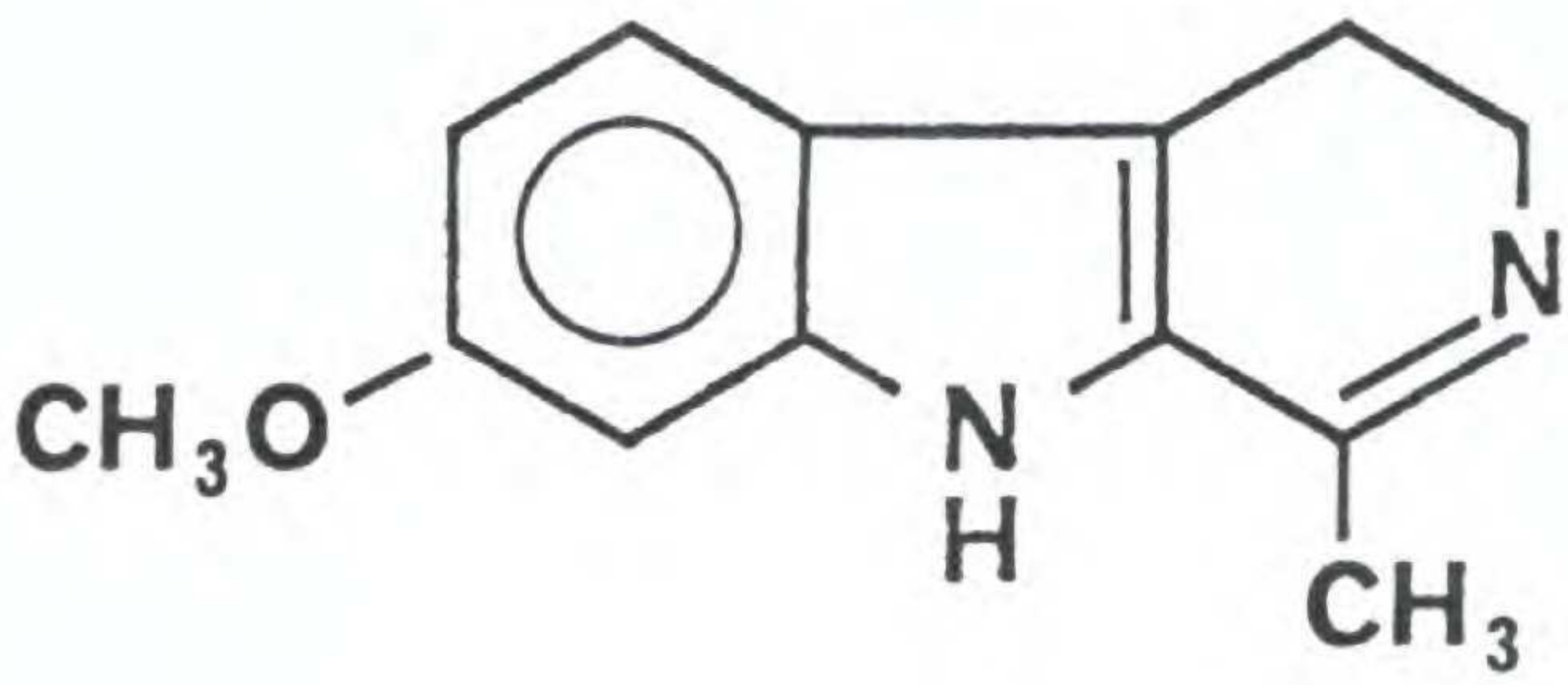
This observation has been often quoted and even misquoted. Additional phytochemical and enzymatic evidence is now available. Trace amounts of β-carbolines have been found to be present in *Virola calophylla, V. theiodora* and *V. elongata* (Fig. 2). In one species, which is not known to be used hallucinogenically, *Virola cuspidata,* harman bases have been found to be the main alkaloids (Fig. 3) (Cassady *et al.* 1971). Their existence has been unequivocally proven by isolation, spectroscopy and mass spectrometry, as compared to synthetic reference compounds. Interestingly, these authors have also observed aromatization due to heat treatment such as that practiced by the Indians when preparing snuff from other species. They also point out the possibility of increased potency of enzyme inhibition due to the aromatization.

Although the monoamineoxidase (MAO) inhibiting properties of harmine were observed indirectly before the enzyme was known to exist (Marinesco *et al.* 1930), it was only through Udenfriend and co-workers (1958) that these properties of the harmala alkaloids could be quantitated. Recently, the structure-activity relationship has been worked out for a large number of β-carbolines (Buckholtz and Boggan 1977). From this work, it is clear that the β-carbolines contained in *Banisteriopsis Caapi* and *Peganum Harmala* are far superior MAO-inhibitors than the compounds contained in usually trace amounts in Virola (Figs. 2–3). Table 2 (from Buckholtz and Boggan) gives a comparison of enzyme inhibitory power.

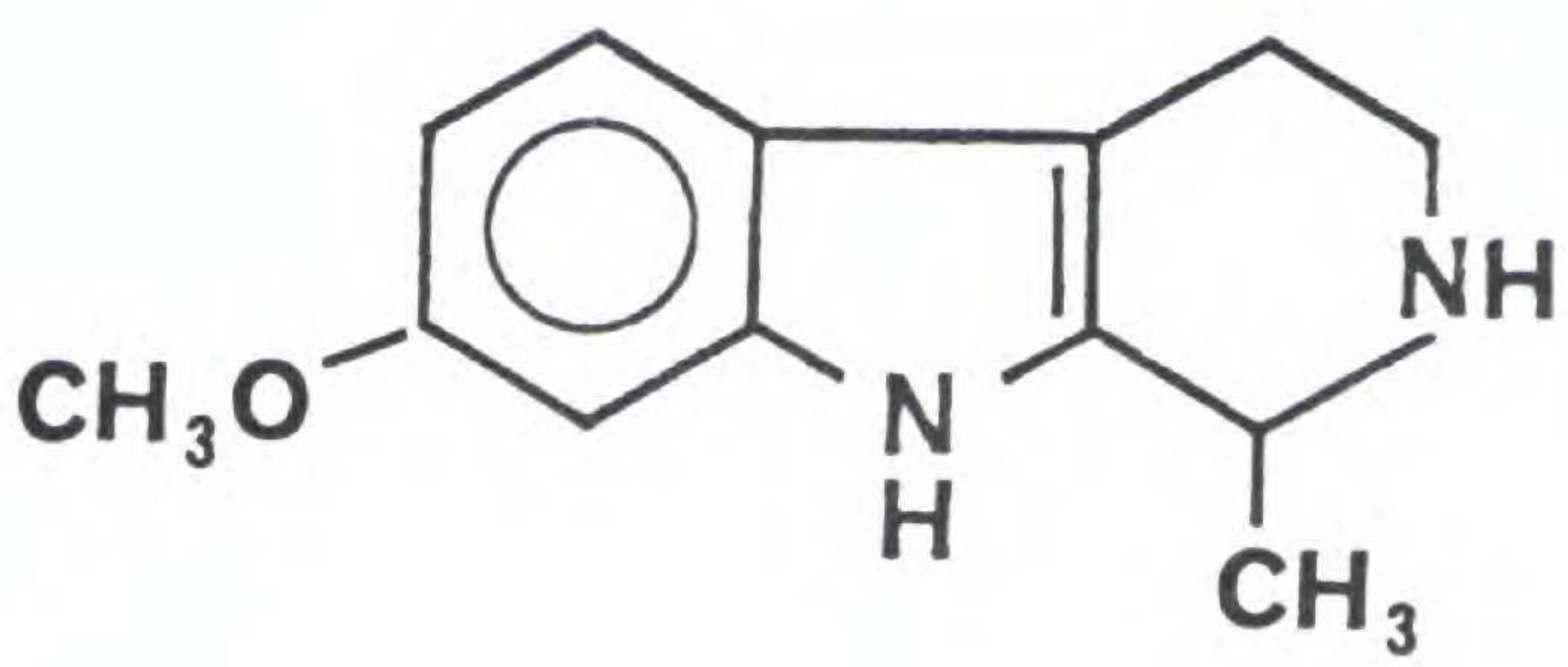
The occurrence of trace amounts of 6-methoxy-β-carbolines in some species of Virola (Table 1 and Fig. 2) is not surprising. It might be expected from the point of view of biosynthesis and workup procedure and is pharmacologically of no importance. The occurrence of a mixture of simple methylated indoles and harmine in one Indian snuff of unknown origin, or of harmine



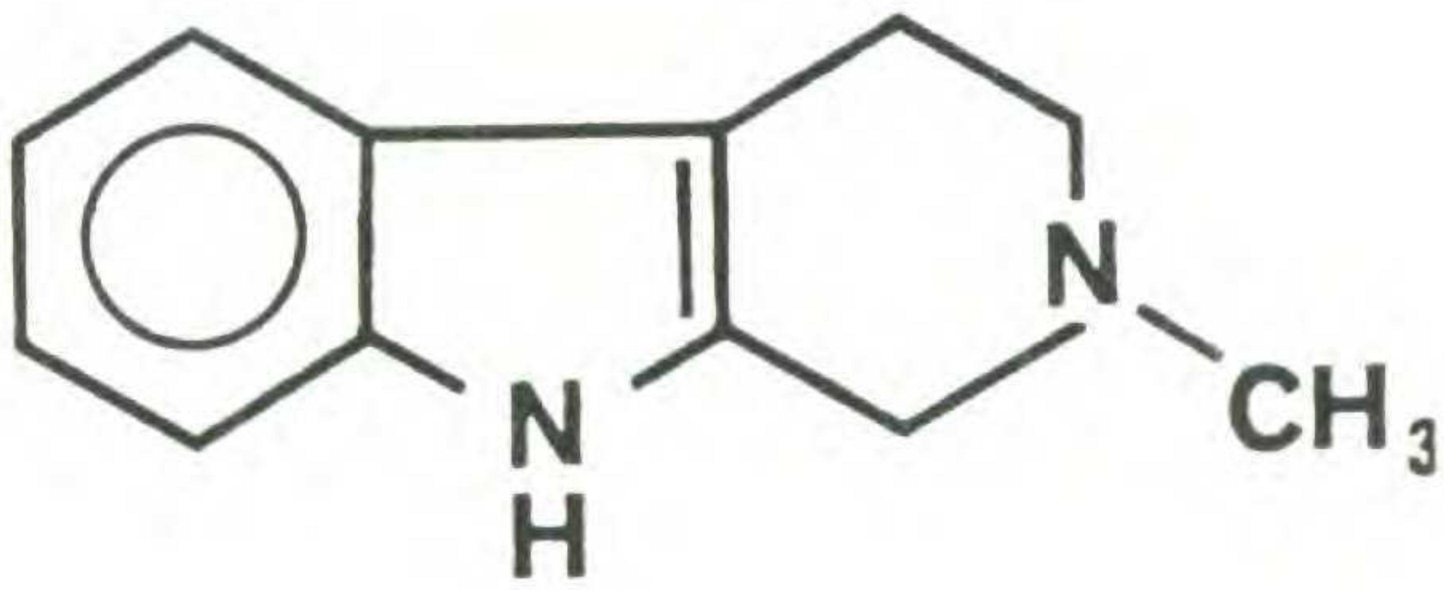
Harmine



Harmaline

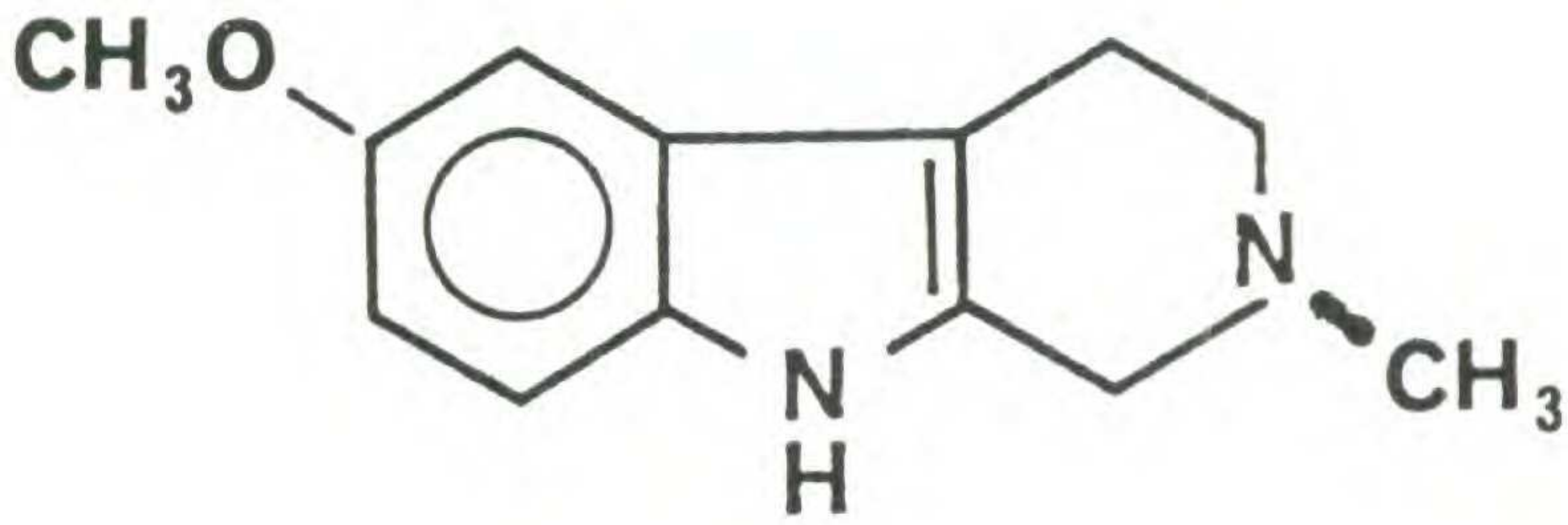


Tetrahydroharmine



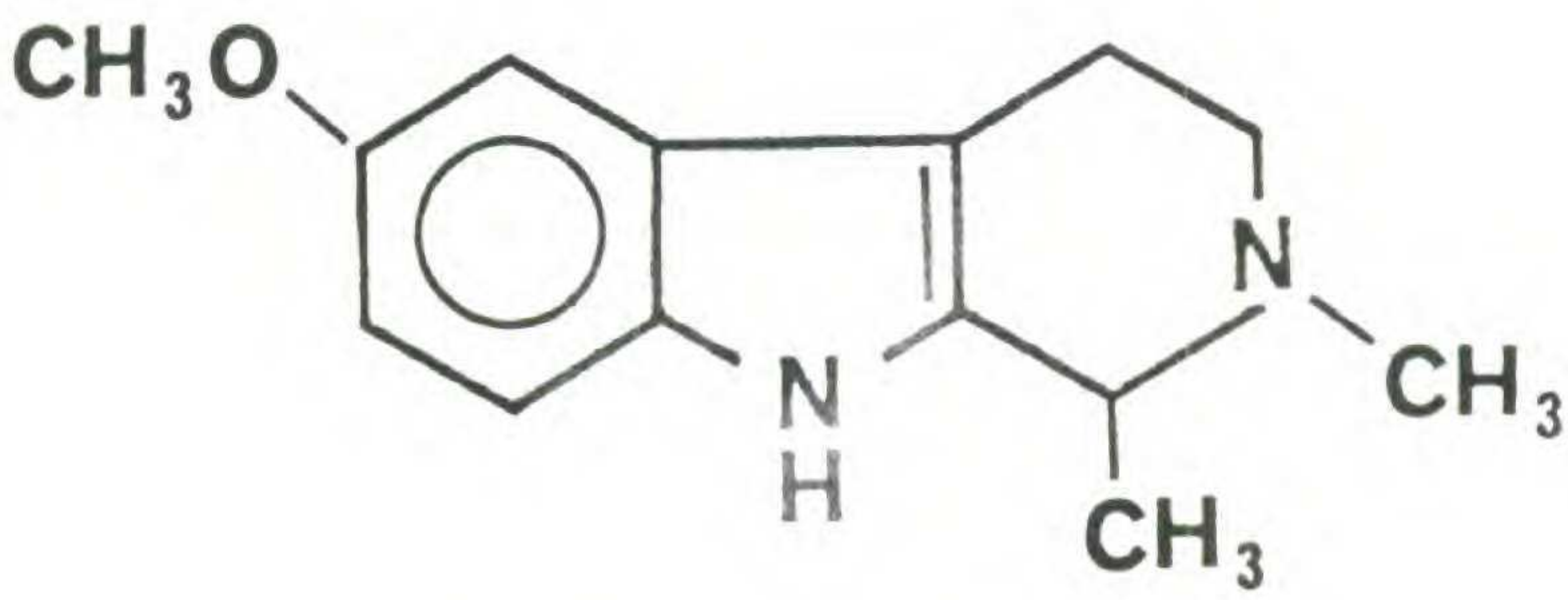
MTHC

2-Methyltetrahydro-
-β-carboline



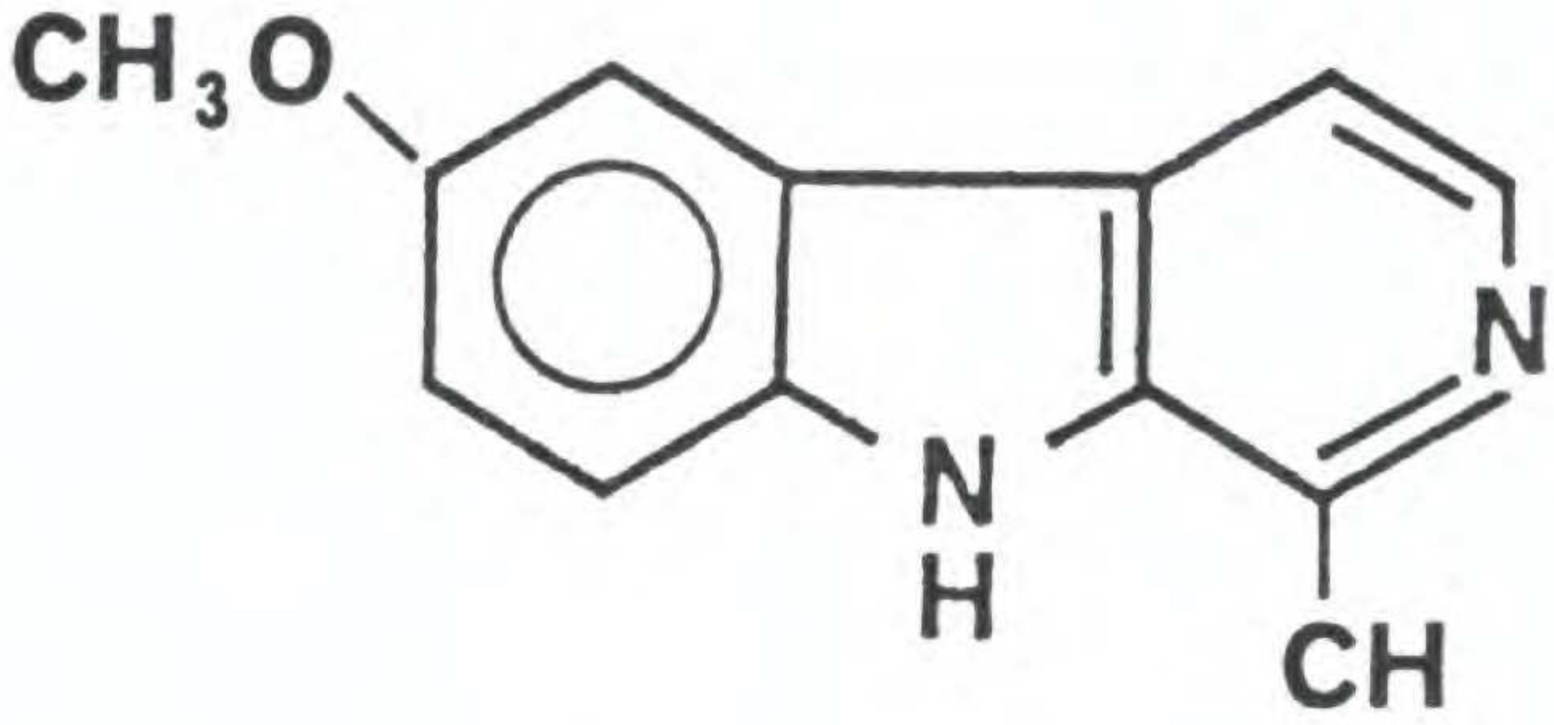
6-MeO-THC

2-Methyl-6-methoxy-
tetrahydro-β-carboline

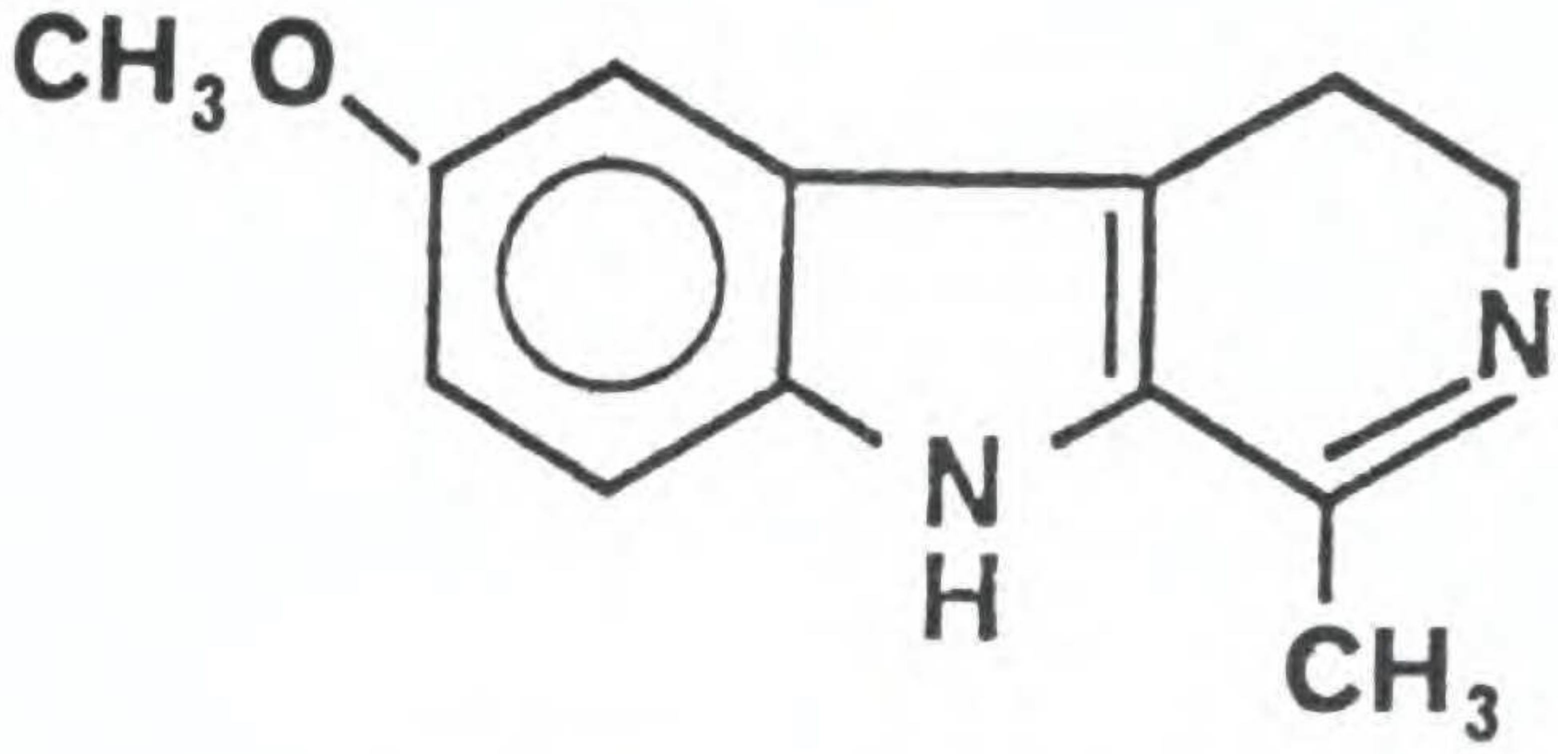


6-MeO-DMTHC

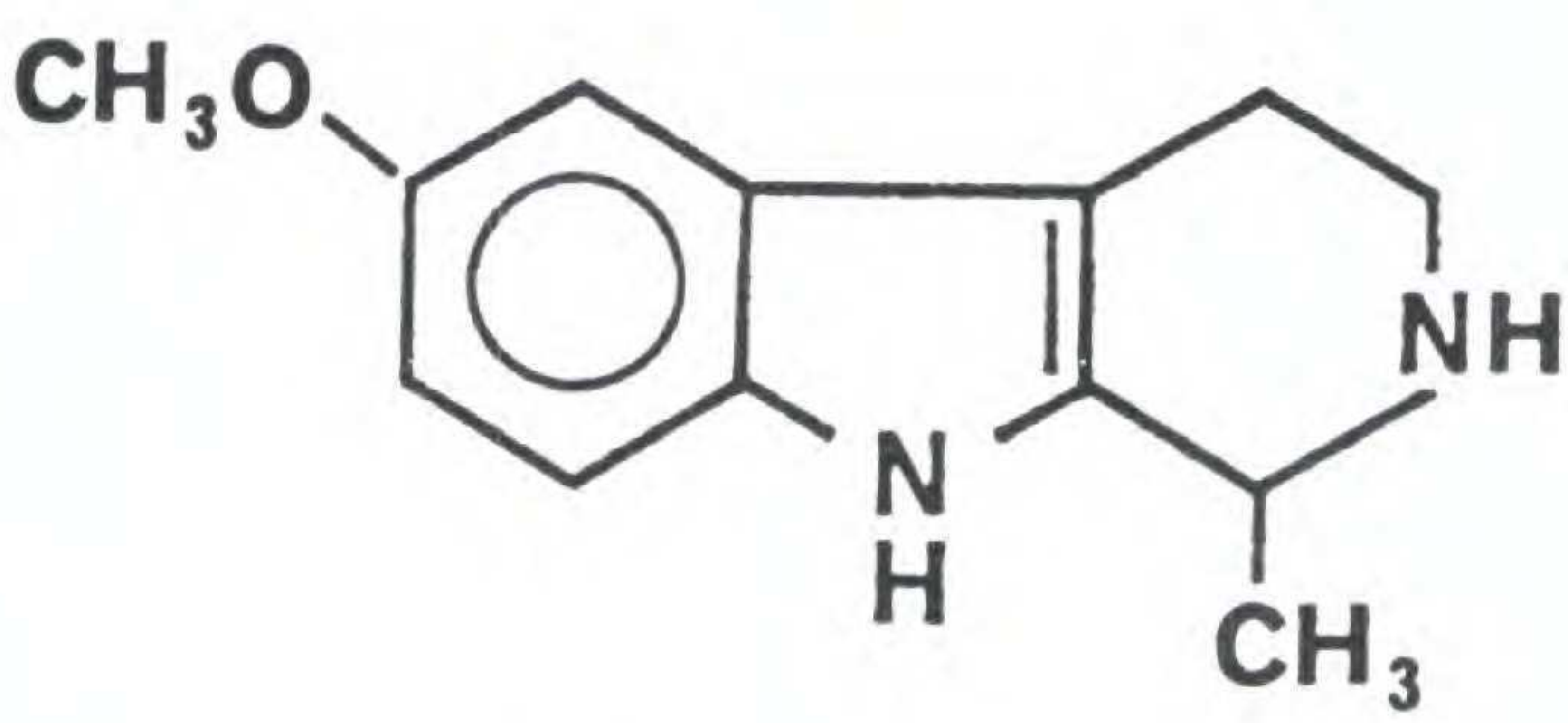
1,2-Dimethyl-6-methoxy-
tetrahydro-β-carbolines



6-Methoxyharmane



6-Methoxyharmalane



6-Methoxytetrahydro-
harmane

Table 2

In vitro inhibition by drugs of the deamination of tryptamine by mouse brain MAO

Drug	EC_{50}(M)
Harmine	8.0×10^{-8}
Harmaline	6.0×10^{-8}
Tetrahydroharmine	1.4×10^{-5}
6-MeO-THC	5.8×10^{-5}
6-MeO-Harmane	3.1×10^{-6}
6-MeO-Harmalane	1.8×10^{-5}
6-MeO-Tetrahydroharmane	4.2×10^{-4}

and related compounds alone in other snuffs, justifies, however, the statement made in 1967 and quoted above and should encourage further research on this interesting group of indigenous drugs and the plants from which they are derived.

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Iryanthera macrophylla (Bth.) Warburg in Nova Acta Acad. Leop.-Carol. 68(1897)155.
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Myristica fragrans Houtt., Handleid 2(1774)333.
Osteophloeum platyspermum (A.DC.) Warburg in Nova Acta Acad. Leop.-Carol. 68(1897)162.
Virola calophylla Warburg in Nova Acta Acad. Leop.-Carol. 68(1897)231.
Virola calophylloidea Markgraf in Repert. Sp. Nov. 19(1923)24.
Virola carinata (Spr. ex Bth.) Warburg in Nova Acta Acad. Leop.-Carol. 68(1897)222.
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Virola multinervia Ducke in Journ. Wash. Acad. Sci. 26(1936)261.
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Virola theiodora (Spr. ex Bth.) Warburg in Nova Acta Acad. Leop.-Carol. 68(1897)187.
Virola venosa (Bth.) Warburg in Nova Acta Acad. Leop.-Carol. 68(1897)224.

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